

Population-based long-term follow-up of patients with myeloproliferative neoplasm: Complications and Prognosis.

Akademisk avhandling

Som för avläggande av medicin doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i Hörsal Arvid Carlsson, Academicum, Medicinargatan 3, Göteborg. Fredagen den 23 februari 2018, klockan 9:00.

av

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Avhandlingen baseras på följande delarbeten

- I. **Abdulkarim K**, Girodon F, Johansson P, Maynadié M, Kutti J, Carli P-M, Bovet E, Andréasson B. AML transformation in 56 patients with Ph- MPD in two well defined populations. *Eur J Haematol*, 2009. **82**(2): p. 106-11
- II. **Abdulkarim K**, Ridell B, Johansson P, Kutti J, Safai-Kutti S, Andréasson B. The impact of peripheral blood values and bone marrow findings on prognosis for patients with essential thrombocythemia and polycythemia vera. *Eur J Haematol*, 2011. **86**(2): p. 148-55.
- III. Bonicelli G, **Abdulkarim K**, Mounier M, Johansson P, Rossi C, Jooste V, Andréasson B, Maynadié M, Girodon F. Leucocytosis and thrombosis at diagnosis are associated with poor survival in polycythaemia vera: a population-based study of 327 patients. *Br J Haematol*, 2013. **160**(2): p. 251-254.
- IV. **Abdulkarim K**, Samuelsson J, Johansson P, Andréasson B. Risk factors for vascular complications and treatment patterns at diagnosis of 2389 PV and ET patients: Real-world data from Swedish MPN registry; *Eur J Haematol*, 2017. **98**(6) p. 577-583.

**SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR MEDICIN.**



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Philadelphia chromosome negative myeloproliferative neoplasms (Ph-MPNs) are rare clonal hematological malignancies mainly, including polycythemia vera (PV), essential thrombocythemia (ET) and myelofibrosis (MF). Patients with these diseases run a high risk of vascular complications and may transform to acute myeloid leukemia (AML). Population-based studies relating to these issues are few in number. The aims were (i) to investigate the rate of AML development in subtypes of Ph-MPNs, (ii) to determine whether clinical and bone marrow findings at diagnosis have an impact on survival and vascular complications in PV and ET, (iii) to find prognostic tools based on clinical findings in newly diagnosed PV and (iv) to describe the “real”- life data from newly diagnosed PV and ET. We have investigated these issues in population-based material; the first and the third studies were based on patients from both Gothenburg, Sweden, and the Côte d’Or area, France, and the second study was population-based from Gothenburg and the fourth study comprised PV and ET patients in the National MPN Registry.

In the median observation period of 15 years, 7% (56 of 795) of patients with Ph-MPN transformed to AML. The yearly rate of AML transformation was significantly higher in MF (1.09%) compared with that of ET (0.37%) and PV (0.38%); ($p = 0.02$ and $p = 0.002$ respectively). Patients with PV had a significantly shorter survival compared with the general Swedish population (HR 1.66; CI:(1.38-1.99); $p < 0.001$). For ET, however, the corresponding survival differences did not reach statistical significance (HR 1.23; CI:(0.97-1.51); $p = 0.089$). Low hemoglobin at the time of diagnosis predicted poor survival in ET ($p = 0.0281$) and splenomegaly predicted poor survival in PV ($p = 0.037$). Using multivariate analysis, independent risk factors at diagnosis for survival in PV patients were identified as: age > 70 years, $WBC > 13 \times 10^9/L$ and thrombotic events. Patients with none of these risk factors had a 10-year relative survival (RS) of 84%, compared with 59% and 26% in patients with one and two or three risk factors respectively.

In the fourth study, we showed that vascular complications preceded MPN diagnosis in 35% of ET and 37% of PV and multivariate analysis identified low hemoglobin as a risk factor for thromboembolic complications in PV ($p = 0.012$), while in ET age > 65 years, $WBC > 12 \times 10^9/L$ and the presence of the JAK2 V617F mutation were independent risk factors ($p = 0.0004$, $p = 0.0038$ and $p = 0.0016$ respectively).

Keywords: essential thrombocythemia, polycythemia vera, myelofibrosis.

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